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10/548,403	07/27/2006	Marie Bendix Hansen	030307-0266	7935

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FOLEY AND LARDNER LLP
SUITE 500
3000 K STREET NW
WASHINGTON, DC 20007

EXAMINER	
KIM, ALEXANDER D	

ART UNIT	PAPER NUMBER
1656	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/548,403	HANSEN ET AL.	
	Examiner	Art Unit	
	ALEXANDER D. KIM	1656	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *08 July 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-15* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-15* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *6/17/2008*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Application Status

1. In response to the previous Office action, a non-Final rejection (mailed on 03/10/2008), Applicants filed a response and amendment received on 07/08/2008. Said amendment amended Claims 1-2, 6-7, 13 and 15.

Claims 1-15 are pending in the instant Office action and will be examined herein.

Information Disclosure Statement

2. Information disclosure statement (IDS) filed on 06/17/2008 has been reviewed, and its references have been considered except for those which have been lined through.

Objections to the Specification

3. The amendment to the specification filed on 7/8/2008 replaces many period symbols with commas in various places, such as the "1.500" into "1,500" in page 3, line 25, for example. The flow rate of fifteen hundred cm/hour is not supported by the original disclosure. The applicant is advised to point out the support in the original disclosure or amend the instant claims.

Appropriate correction is required.

According to MPEP 34 CFR 1.53, "(b) Application filing requirements - Nonprovisional application. The filing date of an application for patent filed under this section, except for a provisional application under paragraph (c) of this section or a

continued prosecution application under paragraph (d) of this section, is the date on which a specification as prescribed by 35 U.S.C. 112 containing a description pursuant to § 1.71 and at least one claim pursuant to § 1.75, and any drawing required by § 1.81(a) are filed in the Patent and Trademark Office. No new matter may be introduced into an application after its filing date. A continuing application, which may be a continuation, divisional, or continuation-in-part application, may be filed under the conditions specified in 35 U.S.C. 120, 121 or 365(c) and § 1.78(a)."

Withdrawn-Claim Objections

4. The previous objection of Claims 2-3 and 14-15 for reciting symbol "l" without being spelled out on its first appearance in the claims is withdrawn by virtue of Applicants' amendment.

Claim Rejections - 35 USC § 112

5. The previous rejection of Claims 1-15 under of 35 U.S.C. 112, second paragraph, for reciting the limitation "a linear flow rate of at least 1.500 cm/hour" is withdrawn by virtue of the examiner's reconsideration.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

New Matter

6. Claims 1-15 are rejected under 35 U.S.C. 112, first paragraph, new matter, as failing to comply with the written description requirement. The claim(s) contain subject matter, which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Instant rejection is necessitated by the instant amendment.

Applicants argue that instant amendment is supported by the paragraph [0061] of US 2007/0092960. However, said paragraph recites "linear flow rates of from about 1.500 (one and half) to 12.000 cm/hr may be applicable during loading of the bio-molecule-containing fluid to the chromatographic column".

Claim 1 (Claims 2-15 dependent therefrom) recites "1,500 cm/hour during loading of the bio-molecule-containing fluid to the chromatographic column" (emphasis added on 1,500 that is fifteen hundred) which limitations are not supported by the original disclosure. The applicant is advised to point out the support in the original disclosure or amend the instant claims.

7. Claim 13 is rejected under 35 U.S.C. 112, first paragraph, new matter, as failing to comply with the written description requirement. The claim(s) contain subject matter, which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed,

had possession of the claimed invention. Instant rejection is necessitated by the instant amendment.

Claim 13 recites "12,000" (i.e., twelve thousand) and "10,000" (i.e., ten thousand) which limitations are not supported by the original disclosure. The applicant is advised to point out the support in the original disclosure or amend the instant claims.

Withdrawn-Claim Rejections - 35 USC § 102

8. The previous rejection of Claims 1, 5-10 and 12-15 under 35 U.S.C. 102(b) as anticipated by Kawakami et al. (US Patent 4,997,914, Mar. 5, 1991) as evidenced by Hirai et al. (US Patent 6,475,478, Nov. 5, 2002), Mitoma et al. (The Journal of Biological Chemistry, volume 276, pages 18060-18065) and Yashida et al. (Biotechnology and Bioengineering, 1994, volume 43, pages 1087-1093) is withdrawn by virtue of instant amendment (i.e., reciting a linear flow rate of at least 1,500 cm/hour).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

9. Claims 1-15 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kawakami et al. (US Patent 4,997,914, Mar. 5, 1991) as evidenced by Hirai et al. (US

Patent 6,475,478, Nov. 5, 2002), Mitoma et al. (The Journal of Biological Chemistry, volume 276, pages 18060-18065), Yashida et al. (Biotechnology and Bioengineering, 1994, volume 43, pages 1087-1093) and Ahern (The Scientist, 1995, Volume 9(22), pages 18, printed as web version).

The rejection was stated in the previous office action as it applied to previous Claims 1-15. In response to this rejection, applicants have amended Claims 1-2, 6-7, 13 and 15; and traverse the rejection as it applies to the newly amended claims.

Applicants argue that the references above do not cure the deficiencies of Kawakami and the examiner has not established a prima facie case of obviousness.

Applicants' arguments have been fully considered but are not deemed persuasive for the following reasons. The examiner acknowledges that Kawakami et al. or other references do not teach the flow rate of 1500 cm/hr. However, as noted below, the prior office action has established a prima facie case of obviousness.

Claim 1 is drawn to a process for isolation of one or more bio-molecule(s) from a bio-molecule containing fluid comprising the steps of: a) optionally adjusting the pH of the bio-molecule-containing fluid; b) bringing the bio-molecule-containing fluid to a temperature of at least 40°C; c) applying a volume of said bio-molecule-containing fluid having a temperature of at least 40°C to an expanded bed adsorption column comprising an adsorbent, said expanded bed column is operated with a linear flow rate of at least 1,500 cm/hour during loading of the bio-molecule-containing fluid to the chromatographic column; d) optionally washing the column; e) eluting at least one bio-

molecule from the adsorbent. Claims 2-15 are drawn to a process of Claim 1 with additional limitation(s) as recited in Claims.

Kawakami et al. teach a process of isolating lactoferrin using a column comprising Cellulofine™ or Chitopearl™ as shown in Examples 1-2, § 4. Kawakami et al. teach method step of applying milk to said column(s) and passing it at a rate of 10 ml/minute (equal to 600 ml/hour, see middle of Example 1, §4) and eluting lactoferrin with 1.0M aqueous sodium chloride solution. It is noted that 10 ml solution volume occupies 3.1 cm in length inside the column with 2 cm diameter, which is the column of Kawakami et al.; thus, the 10 ml/min flow rate of Kawakami et al. would translate into 3.1 cm/min flow rate inside the column of Kawakami et al. The flow rate of Kawakami et al. (i.e., 3.1cm/min = 186 cm/hour) which meets the limitation of recited "a linear flow rate of at least 1.500 cm/hour" in claim 1. Kawakami et al. specifically recites "In the present invention, the contact of the sulfuric ester with raw milk containing lactoferrin is conducted at a temperature of 50°C" (see §2, lines 40-42), which involves step of heating the milk and the column to at least 50°C. It is noted that the column of Kawakami et al. meets the limitation of an expanded bed adsorption column which comprises an adsorbent. Thus, the purification steps of Example 1 or 2 are carried out at 50°C and the method steps of lactoferrin isolation by Kawakami et al. meet all limitations of Claims 1, 6-9 and 13-15. Because the lactoferrin is 80,000 Dalton (see Mitoma et al. Figure 2 on page 18062), the method of Kawakami et al. meets the limitation of Claim 5 reciting a bio-molecule having "at least 1000 Daltons". Hirai et al. teach a Cellulofine available from ChissoCorp. can have a particle diameter of "45 to

105 um"; thus, the Cellulofine™ used in the system of Kawakami et al. meets the limitation of Claims 10-12. The process of Kawakami et al. using Chitopearl™ comprises the step of loading milk on to the column and eluting lactoferrin, which meets the limitation of process of claim 1 in view of reasons stated above. Furthermore, the Chitopearl particle has a density of 390.8 kg/m^3 as a wet particle (see Table 1 of Yoshida et al. 1994, on page 1088). Because the particle is wet, the volume in m^3 (cubic meter) would be comparable to a volume measured in ml to calculate volume, and the density of 390.8 kg/m3 translates into a density of 390800 g/ml, which meets the limitation of claim 12 reciting "a density of at least 1.5 g/ml". Yoshida et al. also teach the particle size is 175 um (i.e., 0.504 x 248.6 um, see Table 1, on page 1068); thus meeting the limitation of Claim 10. Thus, a process taught by Kawakami et al. meets limitations of Claims 1, 5-10 and 12-15.

Kawakami et al. do not teach a process for isolation of a bio-molecule from a bio-molecule containing fluid comprising an expanded bed column that is a large-scale column has at least 10 liter of sedimented adsorbent, has about 50 to 100 liter of sedimented adsorbent or has a diameter of at least 10 cm.

Kawakami et al. do not teach the flow rate of 1,500 cm/hr.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to scale up the size of column to an industrial scale for the production of isolated lactoferrin using the process of Kawakami et al., wherein the industrial scaled column would meet the size and/or the volume as disclosed in Claims 2-3 because "lactoferrin is an iron-binding glycoprotein present in an exocrine liquid

such as milk and has a variety of physiological activities such as bateriostasis against pathogenic bacteria, adjusting function of leukocyte differentiation, build-up function of germicidal power, multiplicative function of lymphocyte and adjusting function of iron absorption" (see §1, lines 13-14) and Kawakami et al. specifically recites the method described above in 35 USC 102 is preferred method in industrial scale because other column such as agarose is soft, which is liable to deforming (see §2, lines 18-22) and cause it to decrease the flow rate (see top of right column of Yoshida et al.). One skilled in the art recognizes that the flow rate can be adjusted by various factors such as the size, shape of column and/or chromatography running condition wherein a faster run time is advantageous in a large industrial scale because Ahern teaches " Because faster flow rates lead to quicker separations with better resolution, liquid chromatography performed under pressure is a powerful analytical and preparative tool for chemists and life scientists" (see middle of page 4 on web printed version, indicated by an arrow). Accordingly, one skilled in the art would have been motivated to use industrial scaled column using the process of Kawakami et al. as described above; wherein the industrial scaled column have appropriate size, shape and/or chromatographic running conditions to have flow rate of at least 1,500 cm/hour; thus, the invention taken as a whole is *prima facie* obvious.

Conclusion

10. Claims 1-15 are not allowed for the reasons identified in the numbered sections of this Office action. Applicants must respond to the objections/rejections in each of the numbered section in this Office action to be fully responsive in prosecution.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to ALEXANDER D. KIM whose telephone number is (571)272-5266. The examiner can normally be reached on 11AM-7:30PM.
If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Kathleen Bragdon can be reached on (571) 272-0931. The fax phone

number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Alexander D Kim/
Examiner, Art Unit 1656

/Richard G Hutson, Ph.D./
Primary Examiner, Art Unit 1652